Epitomes
Important Advances in Clinical Medicine

Allergy

The Scientific Board of the California Medical Association presents the following inventory of items of progress in allergy. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, research workers or scholars to stay abreast of these items of progress in allergy that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Allergy of the California Medical Association and the summaries were prepared under its direction.

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Mental Effects of Long-term Theophylline Therapy in Children

THEOPHYLLINE is the most widely used drug in the United States for the control of chronic asthma. Its use has benefited most persons with this condition. It has an unusually narrow therapeutic index, however, and its use is associated with an increasing number of reports of acute toxic reactions. Central nervous system toxicity occurs with overdosage or by extraneous or intrinsic factors that retard theophylline clearance in patients receiving adequate and proper dosages. Nervousness, restlessness, insomnia, tremors, headaches and convulsions are often noted with high theophylline serum levels.

There have been few reports published of more subtle mental effects, even though many clinicians report cases of such effects anecdotally. Published reports include speech defects; episodic bizarre behavior described as "theophylline madness"; exacerbation of spasticity, depression, behavior or learning problems (or both), and sleep disruption. Considering the widespread use of theophylline, it is surprising that controlled studies have not long since been done of the effects of this drug on brain function.

A retrospective survey has been done of possible adverse behavioral effects of theophylline use in a large group of children with asthma. This showed a significant correlation between theophylline use and inattentiveness, hyperreactivity, irritability and difficult and "withdrawn" behavior.

More recently, in fully controlled trials, theophylline has been shown to adversely affect brain function as measured by a number of sensitive psychological tests such as the Selective Reminding test, the Benton Visual Retention test, the Stroop test and parents' and teachers' child behavior checklists.

In one study a significant improvement in psychological test results occurred when children with asthma were switched from theophylline to cromolyn sodium therapy. These tests reflected visual-spatial planning but were only seen in patients with lower IQ scores (87 to 105) and not in those with IQs in the 111 to 134 range.

Another study showed a correlation between depression and the length of time children had been taking theophylline. The study design, however, did not permit discrimination between an asthma effect or a drug effect as the more likely precipitant.

These and other evaluations have provided evidence that the use of theophylline adversely and significantly affects cognitive ability, especially in terms of short-term memory and concentration, school performance and behavior of some children.

Studies of caffeine intake, which is closely related, have shown that tolerable doses of caffeine in the short term increase the capacity for sustained intellectual effort and decrease reaction time. Higher doses and long-term consumption of caffeine, however, cause a worsening of delicate muscular coordination and accurate timing, restlessness, disturbed sleep and irritability.

The controlled studies of the use of theophylline and the similar well-studied effects of caffeine ingestion question the wisdom of prescribing ongoing theophylline therapy for certain children. It is now clear that physicians need to ask specifically about behavior, school performance and sleeping patterns to assure safety with theophylline and that parents should be advised of possible side effects with its use. A switch to an alternate therapy on a trial basis should be considered in any questionable instance.

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REFERENCES

American Academy of Pediatrics, Section on Allergy and Immunology: Management of asthma. Pediatrics 1981 Dec; 68:874-879